PATENT COOPERATION TREA

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference STRK/P27525PC	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 02/05916	International filing date *(day/month/year)* 24.12.2002	Priority date *(day/month/year)* 24.12.2001
International Patent Classification (IPC) or both national classification and IPC C07D207/34		
Applicant UNIVERSITY OF STRATHCLYDE et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21.07.2003	17.02.2004
Name and mailing address of th international preliminary examining authority: European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer Hass, C Telephone No. +49 30 25901-340

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 02/05916

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-123 as originally filed

Claims, Numbers

1-49 as originally filed

Drawings, Sheets

1/9-9/9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1-15, 29, 31, 32 (all partly); 38-40, 45-47 (with regard to industrial applicability)

   because:

   ☒ the said international application, or the said claims Nos. 38-40, 45-47 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 1-15, 29, 31, 32 are so unclear that no meaningful opinion could be formed *(specify)*:

   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-49
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-49
Industrial applicability (IA)	Yes:	Claims	1-37, 41-44, 48, 49
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 38-40 and 45-47 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

2. Claims 1-15, 29, 31 and 32 have been searched imcompletely for the reasons given on form PCT/ISA/210 as submitted with the international search report. It is pointed out that for these claims an opinion is given only for such subject-matter which has actually been searched.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 Cited documents

D1: US-A-5 698 674 (HE GONG-XIN ET AL) 16 December 1997 (1997-12-16) cited in the application

D2: US-A-5 753 629 (BARALDI PIER GIOVANNI ET AL) 19 May 1998 (1998-05-19) cited in the application

D3: WO 97 28123 A (CALDARELLI MARINA; GERONI MARIA CRISTINA (IT); BERIA ITALO (IT); C) 7 August 1997 (1997-08-07) cited in the application

D4: K. EKAMBARESWARA RAO ET AL: 'Synthesis of Novel Thiazole-Containing Minor Groove Binding Oligopeptides Related to the Antibiotic Distamycin' J. ORG. CHEM., vol. 55, no. 2, 1990, pages 728-737, XP002255609

D5: WO 98 21202 A (BARALDI PIER GIOVANNI; CALDARELLI MARINA (IT); BERIA ITALO (IT)) 22 May 1998 (1998-05-22) cited in the application

D6: US-A-4 912 199 (LOWN J WILLIAM ET AL) 27 March 1990 (1990-03-

27)

D7: US-A-5 273 991 (LEE MOSES N F) 28 December 1993 (1993-12-28) cited in the application

D8: US-A-6 090 947 (BAIRD ELDON ET AL) 18 July 2000 (2000-07-18) cited in the application

D9: US-A-5 637 621 (BOLONICK JOEL ET AL) 10 June 1997 (1997-06-10) cited in the application

D10: EP-A-0 343 893 (PFIZER) 29 November 1989 (1989-11-29)

D11: DWYER T J ET AL: 'DESIGN AND BINDING OF A DISTAMYCIN A ANALOG TO D(CGCAAGTTGGC).D(GCCAACTTGCG): SYNTHESIS, NMR STUDIES, AND IMPLICATIONS FOR THE DESIGN OF SEQUENCE-SPECIFIC MINOR GROOVE BINDING OLIGOPEPTIDES' JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC, US, vol. 114, no. 15, 15 July 1992 (1992-07-15), pages 5911-5919, XP000565675 ISSN: 0002-7863

D12: GUOJIAN XIE ET AL: 'Bisindolylmaleimides Linked to DNA Minor Groove Binding Lexitropsins: Synthesis, Inhibitory Activity against Topoisomerase I, and Biological Evaluation' J. MED. CHEM., vol. 39, no. 5, 1996, pages 1049-1055, XP002255610

V.2 Novelty

V.2.1 The subject-matter of claims 1-48 is novel towards D1 to D11 because of the feature that a branched, cyclic or part cyclic C_{3-5} alkyl group is present as a substituent in a molecule having two or more heterocycles.

V.2.2 It seems that D12, page 1050, figure 1, compounds 2 and 3, destroys the novelty of the subject-matter of claim 49.

V.3 Inventive step

V.3.1 According to the description and with regard to the prior art cited in the international search report, the objective problem underlying the application is to provide further compounds that bind to the minor groove of DNA and which are therefore useful in the pharmaceutical field.

V.3.2 The applicant, in order to solve this problem, has provided compounds which are structurally very similar to the compounds disclosed in documents D1 to D9 and D11. In D1 and in some other of the cited documents there is disclosed that these compounds can bind to the minor groove of DNA. So all of these documents represent relevant prior art.

V.3.3 The disclosure of D1 (compounds having at least three heterocycles which are connected by peptide bonds can bind to minor groove of DNA) is to be seen in connection with the disclosure of, e.g., D2 or D3 or D7, wherein such compounds are described to be useful in the treatment of tumours and viruses. In D7, C_1-C_4 alkyl is possible as substituents at the heterocycles. Here branched alkyl is not excluded, so the feature of the present compounds that these substituents must be branched (or cyclic) must be considered to represent an obvious result from the general possibilities already proposed in the prior art. Since the feature that these substituents are "branched, cyclic or part cyclic C_{3-5} alkyl group(s)" is the only structural difference of the present compounds with regard to the prior art compounds, the subject-matter of the present claims on file (claims 1-49) must be considered not to involve an inventive step.

V.3.4 This objection does not only apply to compound claims 1-32, but also to pharmaceutical use claims 33-47. As to process claim 48 and the claim 49, directed to intermediates, it is stressed that such claims cannot be considered inventive since the end products made from these intermediates by this process are not to be considered inventive.

V.4 Industrial applicability

V.4.1 The subject-matter of claims 1-37, 41-44, 48 and 49 is industrially applicable.

V.4.2 For the assessment of the present claims 38-40 and 45-47 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.